Title:

Efficacy of a Novel Local Prolonged-Release Incisional Doxycycline on Surgical Site Infection Prophylaxis in Abdominal Colorectal Surgery: The SHIELD II Phase 3 Randomized Clinical Trial

Background:

Despite advanced infection control practices, surgical site infections (SSIs) remain a challenge. D-PLEX$_{100}$, a novel Local Prolonged-Release Incisional Doxycycline, was evaluated as an adjunct to standard systemic antibiotic prophylaxis to determine its efficacy in reducing SSIs.

Methods:

SHIELD II was a prospective, randomized, controlled, double-blind, multinational Phase 3 study. Patients undergoing abdominal colorectal surgery with a planned abdominal incision length >20 cm were randomized to D-PLEX$_{100}$ plus standard-of-care (SoC) systemic antibiotics (n=405) or SoC alone (n=393). The primary outcome was a combination of adjudicated incisional SSI, re-intervention at the target incision site, and mortality. Key secondary endpoints included the incidence of adjudicated SSI and ASEPSIS scores >20.

Results:

In the intention-to-treat population, there was a significant 38% risk reduction of the primary efficacy outcome in D-PLEX$_{100}$ arm (10.9%, 44/405) compared with SOC arm (18.1%, 71/393) (ARR 7.2%, 95% CI -12.1 to -2.3; p=0.0039). The incidence of adjudicated incisional SSI indicated a 58% risk reduction in the D-PLEX$_{100}$ arm (3.8% in D-PLEX$_{100}$ vs. 9.5% in SoC; ARR 5.8%, 95% CI -9.3 to -2.3; p=0.0013). Additionally, fewer patients in the D-PLEX$_{100}$ arm had ASEPSIS scores >20 (2.0% in D-PLEX$_{100}$ vs. 5.6% in SoC; p=0.0103). D-PLEX$_{100}$ safety profile did not show significant difference between the groups.

Conclusions:

D-PLEX$_{100}$ in addition to SoC prophylaxis significantly reduced the incidence of incisional SSIs and primary outcome events. These results represent a clinically meaningful improvement in outcomes for patients undergoing major abdominal colorectal surgery and support the incorporation of D-PLEX$_{100}$ into standard prophylactic surgical protocols to reduce SSI-related complications